

Case Report



Range of Varicella Zoster Co-Infections with COVID-19, Singapore

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ABSTRACT

There have been recent descriptions of the novel coronavirus disease 2019 (COVID-19) presenting as 'varicella-like exanthem'. We report three cases of patients with Varicella-Zoster Virus (VZV) and COVID-19 co-infections, presenting in three varied ways. These cases highlight the need for heightened alertness to how such co-infections can present, to pick up overlapping 'dual pathologies' during this current pandemic given that infection control measures including airborne precautions are crucial for both COVID-19 and VZV.

Keywords: COVID-19; Chickenpox; Coinfection; Public health; Communicable diseases

INTRODUCTION

There have been recent descriptions of the novel coronavirus disease (COVID-19) presenting with 'varicella-like exanthema' [1, 2]. Initial queries had been if such papulovesicular eruptions could be herpes simplex virus or varicella zoster virus (VZV) co-manifesting with COVID-19 [3, 4]; though dual simultaneous viral infections would be unusual. Herein we describe 3 patients diagnosed with VZV and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) co-infections with varying presentations.

CASE REPORT

Patient 1, 39-year-old male presented with fever and generalized pruritic vesicular rash of 3 days, in a head-to-centripetal distribution (**Fig. 1A, 1B**). He also tested for nasopharyngeal SARS-CoV-2 by polymerase chain reaction (PCR) (cobas SARS-CoV-2 Test; Roche Molecular Systems, Branchburg, NJ, USA) due to known exposure (Ct value- E gene: 35.76). On day 4 he deteriorated requiring supplemental oxygen. Thoracic imaging showed pulmonary nodules consistent with varicella pneumonia (**Fig. 1C, 1D**). The vesicular fluid tested positive for varicella DNA by PCR (VZV ELITe MGB® Kit; ELITechGroup, Puteaux, France); his sera was VZV IgM and IgG positive.

Patient 2, 24-year-old male presented with 2 days of fever, cough and pruritic vesicular rash, again from a head-to-centripetal distribution. He had potential COVID-19 exposure distinct





Figure 1. Clinical Features of Patients with Varicella and COVID-19 Co-infections.

(A) Clinical Photograph, Patient 1, Vesicular rash on face. (B) Clinical Photograph, Patient 1, Vesicular rash on trunk. (C) Computed Tomography Thorax, Patient 1. (D) Computed Tomography Thorax, Patient 1. (E) Clinical Photograph, Patient 3, Papulo-vesicular rash on face. (F) Clinical Photograph, Patient 3, Papulo-vesicular rash on trunk.

Conflict of Interest

LYAC. is an editorial board member of Infect Chemother, however, he did not involve in the peer reviewer selection, evaluation, and decision process of this article. Otherwise, no potential conflicts of interest relevant to this article was reported.

Author Contributions

Conceptualization: JL, LYAC. Data curation: JL, SMT, LYAC. Investigation: JL, SMT, LYAC. Project administration: JL, SMT, LYAC. Supervision: LYAC. Writing - original draft: JL, SMT, LYAC. Writing - review & editing: JL, SMT, LYAC, PAT, GY, CKL.

from Patient 1 and was SARS-CoV-2 PCR positive (Ct value- E gene: 35.76). The vesicular fluid PCR detected varicella DNA but was negative for SARS-CoV-2.

Patient 3, 32-year-old male had fever and cough for 2 days. He was positive for SARS-CoV-2 via nasopharynx PCR (Ct value- E gene: 35.15), but developed generalized papulo-vesicular rash one week later (**Fig. 1E, 1F**). The patient declined vesicular and blood sampling. Primary varicella was diagnosed clinically based on classical morphological evolution and centripetal distribution.

All the patients had no common epidemiological contact. They were unacquainted; had resided and worked at different locations. All were given acyclovir with improvement. These cases beget the question whether SARS-CoV-2 infection attenuates host immunity, modulates host antiviral lymphocyte function and potentiates susceptibility to opportunistic pathogens [5]. Conversely hyperinflammatory states, recognized in SARS-CoV-2 infection [6], can be a trigger to uncover latent susceptibilities to *Mycobacteria* or *Varicella* [7-9]. However, circulating interleukin-6 incidentally measured for Patient 1 was not elevated at 8.8 pg/mL (normal 1 - 10 pg/mL).



The study was approved by the Institutional Review Board of the National Healthcare Group, Singapore (Approval number: DSRB 2021/00513). Written consent was obtained in each case for use of medical information in this report (Patient 2 declined photo documentation).

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DISCUSSION

We demonstrate the range of clinical presentations in COVID-19-VZV co-infections. Patient 1 had predominant VZV manifestation. Patient 2 had classical VZV skin lesions with upper respiratory symptom from onset. Dermatological presentation of Patient 3 was delayed, one week after COVID-19 diagnosis; similar to patients described by Marzano et al. [1].

Densely-populated locations promote co-transmission of highly infectious pathogens like SARS-CoV-2 and VZV. This can account for occurrence of co-infections epidemiologically short of invoking pathogen-evoked immunomodulation posing public health risks in living spaces like dormitories and community isolation facilities. These cases highlight the need for heightened alertness to pick up overlapping 'dual pathologies' during this current pandemic.

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REFERENCES

1. Marzano AV, Genovese G, Fabbrocini G, Pigatto P, Monfrecola G, Piraccini BM, Veraldi S, Rubegni P, Cusini M, Caputo V, Rongioletti F, Berti E, Calzavara-Pinton P. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: Multicenter case series of 22 patients. J Am Acad Dermatol 2020;83:280-5.

PUBMED | CROSSREF

- 2. Galván Casas C, Català A, Carretero Hernández G, Rodríguez-Jiménez P, Fernández-Nieto D, Rodríguez-Villa Lario A, Navarro Fernández I, Ruiz-Villaverde R, Falkenhain-López D, Llamas Velasco M, García-Gavín J, Baniandrés O, González-Cruz C, Morillas-Lahuerta V, Cubiró X, Figueras Nart I, Selda-Enriquez G, Romaní J, Fustà-Novell X, Melian-Olivera A, Roncero Riesco M, Burgos-Blasco P, Sola Ortigosa J, Feito Rodriguez M, García-Doval I. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol 2020;183:71-7.
- 3. Llamas-Velasco M, Rodríguez-Jiménez P, Chicharro P, De Argila D, Muñoz-Hernández P, Daudén E. Reply to "Varicella-like exanthem as a specific COVID-19-associated skin manifestation: Multicenter case series of 22 patients": To consider varicella-like exanthem associated with COVID-19, virus varicella zoster and virus herpes simplex must be ruled out. J Am Acad Dermatol 2020;83:e253-4.

 PUBMED | CROSSREF



- Ortega-Quijano D, Jimenez-Cauhe J, Burgos-Blasco P, Jimenez-Gomez N, Fernandez-Nieto D. Reply to
 "Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of
 22 patients": Discussing specificity. J Am Acad Dermatol 2020;83:e87.
 PUBMED | CROSSREF
- Zheng M, Gao Y, Wang G, Song G, Liu S, Sun D, Xu Y, Tian Z. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. Cell Mol Immunol 2020;17:533-5.
 PUBMED | CROSSREF
- 6. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033-4.
 - PUBMED | CROSSREF
- 7. Tadolini M, García-García JM, Blanc FX, Borisov S, Goletti D, Motta I, Codecasa LR, Tiberi S, Sotgiu G, Migliori GB; GTN TB/COVID group. On tuberculosis and COVID-19 co-infection. Eur Respir J 2020;56:2002328.
 - PUBMED | CROSSREF
- 8. Fishman JA, Hogan JI, Maus MV. Inflammatory and Infectious Syndromes Associated With Cancer Immunotherapies. Clin Infect Dis 2019;69:909-20.
 - PUBMED I CROSSREF
- 9. Tham SM, Lim WY, Lee CK, Loh J, Premkumar A, Yan B, Kee A, Chai L, Tambyah PA, Yan G. Four Patients with COVID-19 and Tuberculosis, Singapore, April-May 2020. Emerg Infect Dis 2020;26:2764-6.

 PUBMED | CROSSREF